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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,309	03/17/2005	Janet Clark	21226YP	3486

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EXAMINER	
HORLICK, KENNETH R	
ART UNIT	PAPER NUMBER
1637	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/528,309	CLARK ET AL.	
	Examiner	Art Unit	
	Kenneth R. Horlick	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/17/05;6/2/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

2. Claims 8 and 14-16 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. These claims are drawn to kits, but the recited further limitations relate to "intended use" of the kits rather than to the kit components themselves; thus, the claims are not further limiting.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4, and 6-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1 and 2 are confusing because independent claim 1 does not define an active step in part a), which appears to be missing intended language. As a result, although the preamble states that the claim is for "screening a test molecule", no such test molecule is included in the recited method steps. Clarification is required.

B) Claim 4 is confusing because of the language "the methods of claim 3", which lacks proper antecedent basis. Correction is required.

C) Claims 6-20 are confusing because claims 6, 7, 12, and 13 use the language "comprises" whereas it would appear that "comprising" is intended; clarification is required.

D) Claim 16 is further confusing because "the target nucleic acid" lacks proper antecedent basis. Correction is required.

E) Claims 17-20 are further confusing because "the primer" lacks proper antecedent basis; claim 12 refers to "primers". Correction is required.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pecins-Thompson et al. in view of Nielsen et al. (US 5,589,331).

These claims are drawn to a kit comprising a tryptophan hydroxylase (TPH) mRNA riboprobe.

Pecins-Thompson et al. teach a TPH riboprobe; see page 7022 near the bottom of the second column, and Figs. 2 and 3 on page 7024.

This reference does not teach a kit.

The combining of reagents into a kit for the convenience of practicing methods requiring such reagents was conventional in the art at the time of the invention. For example, Nielsen et al. disclose the concept of a kit in column 9 at line 28.

One of ordinary skill in the art would have been motivated to make a kit comprising a TPH riboprobe because such a kit would have clearly been useful in the methods of Pecins-Thompson et al. for detecting expression levels of TPH. With respect to the dependent claims, it is noted that hybridization buffer and *in situ* hybridization methodology were conventional in the art and clearly do not contribute to patentability; also, the concentration of riboprobe is merely a matter of routine optimization and thus does not contribute to patentability. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to make and use the claimed kits.

5. Claims 12-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nielsen et al. (US 5,589,331).

These claims are drawn to a kit comprising tryptophan hydroxylase (TPH) primers.

Nielsen et al. teach TPH primers; see column 10, lines 10-33.

Nielsen et al. teach the concept of a kit in column 9, lines 28.

One of ordinary skill in the art would have been motivated to make a kit comprising TPH primers because such a kit would have clearly been useful in the methods of Nielsen et al. for amplifying TPH nucleic acids. With respect to the dependent claims, it is noted that various amplification buffers, enzymes, and reagents were conventional in the art and clearly do not contribute to patentability; also, the concentration of primers is merely a matter of routine optimization and thus does not contribute to patentability. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to make and use the claimed kits.

6. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bethea et al. (2000, Novartis Foundation Symposium) in view of Harpold et al. (US 5,401,629).

These claims are drawn to methods of screening a test molecule for ERβ agonist activity comprising: determining the level of TPH gene transcription in a biological sample contacted with said molecule using either a riboprobe (claims 1-2) or primers and RT-PCR (claims 3-5), and comparing said level with a control level, wherein an

increase in said level relative to the control level indicates ERβ agonist activity of the test molecule.

Bethea et al. teach that estrogen, acting via the ERβ receptor, causes an increase in TPH transcription (see abstract on page 112). Bethea et al. also teach TPH riboprobes and primers near the bottom of page 117, as well as RT-PCR.

Bethea et al. do not teach screening a test molecule for ERβ agonist activity.

Harpold et al. disclose the desirability of screening for test compounds of therapeutic value which have agonist or antagonist activity with respect to cell surface receptors (see columns 1-2).

One of ordinary skill in the art would have been motivated to apply the teaching of Bethea et al. regarding increased TPH expression via the ERβ receptor to a screening assay for test compounds having ERβ agonist activity because as taught by Harpold et al., it was desirable to screen for and obtain drugs having agonist and antagonist activity with respect to cell surface receptors for therapeutic treatment. The clinical importance of estrogen and thus its receptors was well known in the art at the time of the invention, and is mentioned by Bethea et al. Considering Harpold et al., the correlation between ERβ and increased TPH expression taught by Bethea et al. would have been suggestive of an assay means for screening for agonists and antagonists of ERβ which would be of potential therapeutic value. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods.

7. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pecins-Thompson et al., in view of any one of Lu et al. (1999), Gundlah et al. (2001), or Bethea et al. (2002), and further in view of Harpold et al. (US 5,401,629).

These claims are drawn to methods of screening a test molecule for ERβ agonist activity comprising: determining the level of TPH gene transcription in a biological sample contacted with said molecule using either a riboprobe (claims 1-2) or primers and RT-PCR (claims 3-5), and comparing said level with a control level, wherein an increase in said level relative to the control level indicates ERβ agonist activity of the test molecule.

Pecins-Thompson et al. teach that estrogen, likely acting via its receptor, causes an increase in TPH transcription (see entire document on pages 7021-7029). This reference also teaches a TPH riboprobe and TPH primers; see page 7022, second column, and Figs. 2 and 3 on page 7024.

Pecins-Thompson et al. do not teach a correlation between the specific estrogen receptor ERβ and increased TPH expression, nor a screening assay for a test molecule for ERβ agonist activity.

Each of the secondary references teaches a correlation between ERβ and increased TPH expression (in Lu et al. see pages 257-267; in Gundlah et al. see pages 14-22, and in Bethea et al. see pages 431-445).

Harpold et al. disclose the desirability of screening for test compounds of therapeutic value which have agonist or antagonist activity with respect to cell surface receptors (see columns 1-2).

One of ordinary skill in the art would have been motivated to apply the teaching of Pecins-Thompson et al. regarding increased TPH expression by estrogen, to ERβ, because each of the secondary references suggested that the action of estrogen was mediated by ERβ. The skilled artisan would have been further motivated to apply the teachings of the noted references to a screening assay for test compounds having ERβ agonist activity because as taught by Harpold et al., it was desirable to screen for and obtain drugs having agonist and antagonist activity with respect to cell surface receptors for therapeutic treatment. The clinical importance of estrogen and thus its receptors was well known in the art at the time of the invention, and is mentioned by the primary and secondary references. Considering Harpold et al., the correlation between ERβ and increased TPH expression taught by the primary and secondary refernces would have been suggestive of an assay means for screening for agonists and antagonists of ERβ which would be of potential therapeutic value. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods.

8. Bethea et al. (2000, Biological Psychiatry) and Gundlah et al. (2005) are made of record as references of interest.

9. No claims are free of the prior art.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kenneth R. Horlick whose telephone number is 571-272-0784. The examiner can normally be reached on Monday-Thursday 6:30AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kenneth R. Horlick, Ph.D.
Kenneth R Horlick
Primary Examiner
Art Unit 1637

03/14/07